

3. An EPO form of claim 2 having an extended serum half-life
4. An EPO form of claim 3, wherein said extended serum half-life is greater than 20 hours.

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5. The fusion proteins (iv), (vi) or (viii) of claim 1, wherein said fusion proteins have greater specific activity than the comparable Fc-EPO fusion proteins having no mutated EPO molecules.

- 10 6. A fusion protein of claim 5, wherein in the EPO_m portion at least one of the following changes is achieved:

Asn_{24, 38, 83} → Gln, Ser₁₂₆ → Ala, His₃₂ → Gly, Ser₃₄ → Arg, Pro₉₀ → Ala.

- 15 7. The fusion proteins (ix) and (x) of claim 1, wherein EPO_{trunc} has an amino acid sequence which ends C-terminally with the amino acid positions 108, 98, 93, 88, 85 or 77 of EPO or EPO_m.

8. A fusion protein of claim 1, wherein the mutation of the Fc_m portion causes reduced affinity to Fc receptors.

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9. A fusion protein of claim 1, wherein the linker L is $(\text{Gly}_4\text{Ser})_x$, $x = 1 - 4$.

Claim 1

10. A fusion protein of any of the claims 1-9, wherein at least one of the cysteine residues of the EPO molecule or EPO_m molecule is engineered.

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11. A fusion protein of claim 10 wherein the EPO moiety has a pattern of disulfide bonding distinct from human or mammalian erythropoietin.

Sub A2

- 30 12. A fusion protein of claim 10 or 11 or a non-fused EPO of claim 1, wherein the EPO includes at least one of the following amino acid variations: position 29 is not Cys, position 33 is not Cys, position 88 is Cys, position 139 is Cys.

Claim 10

13. A fusion protein or a non-fused EPO of any of the claims 10-12, wherein said engineered cysteine residues form a disulfide bond.

a 14. A fusion protein or a non-fused EPO according to claim 12 ~~or 13~~, wherein the EPO is derived from human EPO and has at least one of the following mutations: His₃₂ → Gly, Ser₃₄ → Arg and Pro₉₀ → Ala.

a 5 15. A fusion protein according to ^{claim 1} ~~any of the claims 1-14~~, wherein the EPO portions or EPO_m portions within the Fc fusion protein are dimerized.

a 16. A fusion protein according to ^{claim 1} ~~any of the claims 1-15~~, said fusion protein being a whole Ig molecule.

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17. A fusion protein according to ^{claim 1} ~~any of the claims 1-16~~, wherein the Ig molecule and the EPO molecule is of mammalian origin.

18. A fusion protein of claim 17, wherein the Ig molecule is human IgG.

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a 19. A DNA sequence encoding any of the EPO forms of ^{claim 1} ~~claims 1-18~~.

20. A DNA molecule encoding a fusion protein of claim 1 comprising:

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(a) a signal / leader sequence

(b) a Fc region of an Ig molecule

(c) a target protein sequence having the biological activity of erythropoietin.

a 21. An expression vector comprising a DNA of claim 19 ~~or 20~~.

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22. A host cell suitable for expressing an EPO form as defined in claim 1 comprising a vector of claim 21.

23. A method for producing a fusion protein of claim 1, said method comprising:

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(i) constructing a DNA encoding a precursor protein that comprises from N-terminus to C-terminus a leader sequence for secretion, the Fc portion and the EPO, EPO_m or EPO_{trunc},

(ii) placing said fused DNA in an appropriate expression vector,

(iii) expressing said fusion protein in a eukaryotic cell, and

(iv) purifying said secreted fusion protein.

Sub-A3
Sub-B1

